ELITRA.001DV1 PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

#12/K.T. 11/8 ELECT. A

Applicant	:	Zyskind, et al.	Group Art Unit 1635
Appl. No.	:	09/912,020	
Filed	:	July 23, 2001	
For	:	GENES IDENTIFIED AS REQUIRED FOR PROLIFERATION IN ESCHERICHIA COLI	
Examiner	:	Angell, J.	

I hereby certify that this correspondence and all marked attachments are being deposited with the United States Postal Service as first-class mail in an envelope addressed to: United States Patent and Trademark Office, P.O. Box 2327, Arlington, VA 22202, on

November 1, 2002
(Date)

Daniel Hart
Daniel Hart, Reg. No. 40,637

RESPONSE TO RESTRICTION REQUIREMENT

United States Patent and Trademark Office
P.O. Box 2327
Arlington, VA 22202

Dear Sir:

This is a response to the Restriction Requirement mailed on October 1, 2002 (Paper Number 10) in connection with the above-identified application. Applicants provisionally elect the polypeptide sequence of SEQ ID NO: 325 with traverse due to the biological interrelationships between certain sequences. Additionally, Applicants respectfully request entry of the following amendments and consideration of the following remarks.

IN THE CLAIMS

Please amend claims 1, 4, 6, 7, 11, 13 and 14 as follows. Please add new claims 18-20.

1. (Amended) A method of inhibiting cellular proliferation comprising inhibiting the activity or reducing the amount of a polypeptide comprising the amino acid sequence of SEQ ID NO: 325 or inhibiting the activity or reducing the amount of a nucleic acid encoding said polypeptide.

4. (Amended) A method for inhibiting cellular proliferation comprising introducing a compound which inhibits the activity or reduces the amount of a polypeptide comprising the amino acid sequence of SEQ ID NO: 325 or which inhibits the activity or reduces the amount of a nucleic acid comprising a nucleotide sequence encoding said polypeptide into a cell.

6. (Amended) The method of Claim 5, wherein said compound is an antisense nucleic acid comprising a sequence selected from the group consisting of SEQ ID NOs: 459 and 460, or a proliferation-inhibiting portion thereof.

7. (Amended) The method of Claim 6, wherein said proliferation inhibiting portion of one of SEQ ID NOs: 459 or 460 is a fragment comprising at least 10, at least 20, at least 25, at least 30, at least 50 or more than 50 consecutive nucleotides of one of SEQ ID NOs: 459 or 460.

11. (Amended) A method for inhibiting cellular proliferation comprising introducing a compound with activity against a gene corresponding to one of SEQ ID NO: 165 or with activity against the product of said gene into a population of cells expressing a gene.

13. (Amended) The method of Claim 12, wherein said compound is an antisense oligonucleotide comprising a sequence selected from the group consisting of SEQ ID NOs: 459 and 460, or a proliferation-inhibiting portion thereof.

14. (Amended) The method of Claim 13, wherein said proliferation inhibiting portion of one of SEQ ID NOs: 459 or 460 is a fragment comprising at least 10, at least 20, at least 25, at least 30, at least 50 or more than 50 consecutive nucleotides of one of SEQ ID NOs: 459 or 460.

18. (New) The method of Claim 1, wherein the cell in which proliferation is inhibited is selected from the group consisting of *Escherichia coli*, *Pseudomonas aeruginosa*, *Enterobacter cloacae*, *Helicobacter pylori*, *Neisseria gonorrhoeae*, *Haemophilus influenzae*, *Salmonella typhimurium*, *Salmonella typhi*, *Salmonella paratyphi*, *Salmonella cholerasuis*, *Klebsiella pneumoniae*, *Yersinia pestis*, and *Campylobacter jejuni* or any species falling within the genera of any of the above species.

19. (New) The method of Claim 4, wherein the cell in which proliferation is inhibited is selected from the group consisting of *Escherichia coli*, *Pseudomonas aeruginosa*,

Enterobacter cloacae, Helicobacter pylori, Neisseria gonorrhoeae, Haemophilus influenzae, Salmonella typhimurium, Salmonella typhi, Salmonella paratyphi, Salmonella cholerasuis, Klebsiella pneumoniae, Yersinia pestis, and *Campylobacter jejuni* or any species falling within the genera of any of the above species.

20. (New) The method of Claim 11, wherein the cell in which proliferation is inhibited is selected from the group consisting of *Escherichia coli, Pseudomonas aeruginosa, Enterobacter cloacae, Helicobacter pylori, Neisseria gonorrhoeae, Haemophilus influenzae, Salmonella typhimurium, Salmonella typhi, Salmonella paratyphi, Salmonella cholerasuis, Klebsiella pneumoniae, Yersinia pestis,* and *Campylobacter jejuni* or any species falling within the genera of any of the above species.

REMARKS

Claims 1, 4, 6, 7, 11, 13 and 14 have been amended to recite a specific SEQ ID NO corresponding to the WaaE polypeptide, a specific SEQ ID NO corresponding to the *waaE* gene, or two overlapping SEQ ID NOs corresponding to antisense nucleic acids complementary to at least a portion of the *waaE* gene. Applicants make each of the above amendments without prejudice or disclaimer. New claims 18-20, which are dependent on claims 1, 4 and 11, respectively, have also been added. Accordingly, claims 1-20 are currently pending.

SUPPORT FOR CLAIM AMENDMENTS

Support for the amendments to claims 1, 4, 6, 7, 11, 13 and 14 and new claims 18-20 is present in the claims as originally filed and throughout the specification. Accordingly, no new matter has been added to this application.

SEQUENCE ELECTION REQUIREMENT

Applicants have provisionally elected the polypeptide of SEQ ID NO: 325 for further prosecution; however, Applicants respectfully traverse the requirement which limits examination of the elected claim set with respect to only one sequence due to the biological interrelationships between the sequences recited in the claims as amended above.

Applicants respectfully submit that the polypeptide of SEQ ID NO: 325, the coding nucleic acid of SEQ ID NO: 165 and the two overlapping antisense nucleic acids of SEQ ID

NOs: 459 and 460 can be searched and examined together without undue burden because of their biological interrelationship. Applicants have discovered that expression of either of the antisense nucleic acids of SEQ ID NOs: 459 or 460, which are complementary to at least a portion of the *waaE* gene, inhibits cellular proliferation, thereby indicating that the gene of SEQ ID NO: 165 (*waaE*) and its respective encoded protein of SEQ ID NO: 325 (WaaE) are essential for cellular proliferation. In view of this essentiality, the antisense nucleic acids of SEQ ID NOs: 459 and 460, the gene of SEQ ID NO: 165 and the polypeptide of SEQ ID NO: 325 can be used in methods claimed in the instant application. In addition, Applicants respectfully submit that no searching burden is created by examination of each of the foregoing sequences in the present application since it is sufficient for patentability to simply verify the novelty of Applicants' discovery that *waaE* is an essential microbial gene. In view of the foregoing biological interrelationships, Applicants respectfully request that the essential polypeptide of SEQ ID NO: 325, the essential gene of SEQ ID NO: 165 and the antisense nucleic acids of SEQ ID NOs: 459 and 460 be searched and examined together.

In addition to the interrelationships between antisense, sense and polypeptide sequences, Applicants note that the two antisense nucleic acids of SEQ ID NOs: 459 and 460 are related to each other by both structure and function. In particular, the nucleic acids of SEQ ID NO: 459 (300 nucleotides in length) and SEQ ID NO: 460 (293 nucleotides in length) overlap each other by 205 nucleotides. Furthermore, each of these antisense nucleic acids have the similar function of inhibiting cellular proliferation by reducing the level or activity of the product of the *waaE* gene. In light of the foregoing, Applicants respectfully submit that each of the sequences described herein show sufficient relationship to each other that they can be examined together and that the examination of each of these sequences in the present application does not place a burden on the Examiner.

CONCLUSION

Should the Examiner have any questions regarding the present response to the restriction requirement, he is invited to contact the undersigned at the telephone number provided below.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: Nov. 1, 2002

By: Daniel Hart

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS

1. (Amended) A method of inhibiting cellular proliferation comprising inhibiting the activity or reducing the amount of a polypeptide comprising**[a]** the amino acid sequence **[selected from the group consisting]** of **[SEQ ID NOs. 243-357 and SEQ ID NOs. 359-398]** SEQ ID NO: 325 or inhibiting the activity or reducing the amount of a nucleic acid encoding said polypeptide.

4. (Amended) A method for inhibiting cellular proliferation comprising introducing a compound which inhibits the activity or reduces the amount of a polypeptide comprising**[a]** the amino acid sequence **[selected from the group consisting]** of **[SEQ ID NOs. 243-357 and SEQ ID NOs. 359-398]** SEQ ID NO: 325 or which inhibits the activity or reduces the amount of a nucleic acid comprising a nucleotide sequence encoding said polypeptide into a cell.

6. (Amended) The method of Claim 5, wherein said compound is an antisense nucleic acid comprising a sequence selected from the group consisting of **[SEQ ID NOs.: 405-485]** SEQ ID NOs: 459 and 460, or a proliferation-inhibiting portion thereof.

7. (Amended) The method of Claim 6, wherein said proliferation inhibiting portion of one of **[SEQ ID NOs. 405-485]** SEQ ID NOs: 459 or 460 is a fragment comprising at least 10, at least 20, at least 25, at least 30, at least 50 or more than 50 consecutive nucleotides of one of SEQ ID NOs: **[405-485]** 459 or 460.

11. (Amended) A method for inhibiting cellular proliferation comprising introducing a compound with activity against a gene corresponding to one of **[SEQ ID NOs.: 82-242]** SEQ ID NO: 165 or with activity against the product of said gene into a population of cells expressing a gene.

13. (Amended) The method of Claim 12, wherein said compound is an antisense oligonucleotide comprising a sequence selected from the group consisting of **[SEQ ID NOs.: 405-485]** SEQ ID NOs: 459 and 460, or a proliferation-inhibiting portion thereof.

14. (Amended) The method of Claim 13, wherein said proliferation inhibiting portion of one of **[SEQ ID NOs. 405-485]** SEQ ID NOs: 459 or 460 is a fragment comprising at

least 10, at least 20, at least 25, at least 30, at least 50 or more than 50 consecutive nucleotides of one of SEQ ID NOs: **[405-485]** 459 or 460.

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PATENT

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UNITED STATES PATENT AND TRADEMARK OFFICE
P.O. Box 2327
Arlington, VA 22202

Sir:

Transmitted herewith is the response to the restriction requirement in the above-identified application.

The fee has been calculated as shown below:

CLAIMS AS FILED

	CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NO. PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE	ADDITIONAL FEE
Total Claims	20	—	20	= 0 ×	$9	= $0
Independent Claims	3	—	3	= 0 ×	$42	= $0
If application has been amended to contain multiple dependent claim(s), then add					$140	= $0
Time Extension Fee						$0
TOTAL ADDITIONAL FEE FOR THIS AMENDMENT						$0

(X) The present application qualifies for small entity status under 37 C.F.R. § 1.27.

(X) Return prepaid postcard.

(X) Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

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